REMARKS

Claims 1-27, 30-34, 47, 48, 50 and 57-60 are pending in this application.

Applicants have amended claims 1 and 47 to recite that the formed permanent cartilage is stable and not subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device. Support for these claims is provided, e.g., on page 24, lines 22-24 of the specification.

Applicants address the Examiner's objections and rejections below:

THE OBJECTIONS

Specification

The Examiner has objected to the specification stating that trademarks are disclosed throughout the instant specification and that not all of them are capitalized or accompanied by the generic terminology.

Applicants have amended the specification at page 3, line 22 to page 4, line 7; page 21, lines 3-12; page 32, lines 2-14; page 33, lines 1-22; page 38, lines 15-21; page 38, line 22 to page 39, line 1; page 41, lines 4-12; page 41, lines 13-22; page 41, line 24 to page 42, line 3; and page 42, lines 5-16 to correctly identify all trademarks. Accordingly, applicants request that the Examiner withdraw this objection.

THE REJECTIONS

35 U.S.C. § 132

The Examiner has rejected applicants' amendment filed November 8, 2004 under 35 U.S.C. § 132 stating that the amendment introduces new matter into the disclosure of the invention. Specifically, the Examiner asserts that there is no support in the original disclosure for the recitation of "wherein said formed permanent cartilage does not undergo resorption." The Examiner suggests that applicants replace the phrase with the statement found on page 24, lines 22-24. Accordingly, applicants have amended claims 1 and 47 to recite that the formed permanent cartilage is stable and not subject to resorption, as evidenced

by the continued existence of cartilage at 4 months post implantation of the osteogenic device. In view of the amendment, applicants request that the Examiner withdraw this rejection.

35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-27, 30-34, 47, 48, 50 and 57-60 under 35 U.S.C. § 112, first paragraph for lack of written description. Specifically, the Examiner contends that the claims recite added material which is not supported by the original disclosure. The Examiner states that the language "wherein said formed permanent cartilage does not undergo resorption" is not supported by the instant application. The Examiner suggests that applicants replace the phrase with the statement found on page 24, lines 22-24 of the specification.

Applicants have amended claims 1 and 47 (and therefore, claims dependent therefrom) as suggested by the Examiner, thus, obviating the rejection.

35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-27, 30-34 and 57-60 under 35 U.S.C. § 112, second paragraph for lack of definiteness. Specifically, the Examiner contends that the recitations of "bioresorbable" and "does not undergo resorption" in claim 1 are confusing and inconsistent. Applicants traverse.

Applicants respectfully submits that the term "bioresorbable" in claim 1 is used to describe the carrier in which the osteogenic protein is disposed in and not the newly formed permanent cartilage. Accordingly, there is no inconsistency in the claims and applicants request that the Examiner withdraw the indefiniteness rejection.

35 U.S.C. § 103(a)

Claims 1-25, 27, 30-34, 47-48, 57, and 59-60

The Examiner has maintained the rejection of claims 1-25, 27, 30-34, 47-48, 57, and 59-60 under 35 U.S.C. § 103(a) as being obvious over WO 96/14335 ("Luyten") in view of WO 95/16035 ("Celeste") and Cui et al., "Repair of thyroid cartilage defect

with bone morphogenetic protein," Annals of Otology, Rhinology and Laryngology, 106, pp. 326-328 (1997) ("Cui"). The Examiner states that Luyten discloses CDMP-1 and CDMP-2 having *in vivo* chondrogenic activity and that the CDMPs may be combined with a fibrin glue, cartilage grafts and collagens. The Examiner states that Celeste teaches BMPs are useful in the treatment of tendon or ligament defects and in the formation of bone, cartilage and tendon, as well as pharmaceutical acceptable carriers such as collagen, PLA, PGA and CMC. The Examiner further states that Cui teaches the repair of thyroid cartilage defect with BMPs. The Examiner, therefore, concludes that it would have been obvious to one skilled in the art to arrive at the claimed invention by combining the teachings of the cited references.

The Examiner states the applicants' response filed November 8, 2004 has been considered but that it did not address the art rejections of record. The Examiner states that he is assuming that applicants would have reiterated the arguments previously presented in previous amendments filed. The Examiner also states that the limitations recited in the claims do not

obviate the art rejections as the cited prior art teach the same carrier, thus has the same properties, see for example pages 3-4 of the instant specification. Applicants traverse.

First, applicants respectfully submit that in their November 8, 2004 Reply and Amendment Accompanying Request for Continued Examination, they stated on page 1 that applicants are providing the following remarks which are supplementary to applicants' September 8, 2004 Reply. Therefore, applicants had requested that the Examiner consider the November 8, 2004 Reply in conjunction with their September 8, 2004 Reply, in which applicants had addressed the art rejections of record.

Second, applicants respectfully submit that the amended claims of the instant application require that functional permanent replacement cartilage tissue be induced and that such permanent cartilage is stable and not subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device. This essential feature of the invention is not disclosed in Luyten, Celeste or Cui, either alone or in combination.

Luyten discloses that BMPs may have cartilage and bone inducing activity. However, the disclosure in Luyten relating to the cartilage inductive activity is in the context of the stages of endochondral bone formation. Specifically, Luyten states that the normal stages of endochondral bone formation "include mesenchymal condensation, cartilage, and bone marrow formation and eventual mineralization to produce mature bone" (see, page 1, lines 25-27). There is no teaching or suggestion in Luyten that the formed cartilage is stable and not subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device. In fact, Luyten teaches away from the present invention by stating that the formed cartilage is mineralized to form bone. Therefore, in contrast with the amended claims of the instant application which require permanent cartilage formation wherein such permanent cartilage is stable and not subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device, the cartilage formation disclosed in Luyten is a transient intermediate step in the process of endochondral bone formation.

Neither Cui nor Celeste remedies this deficiency. Cui discloses that bovine BMP repairs a thyroid cartilage defect by inducing new bone formation which fills the defect in the cartilage. Cui teaches that although both new bone and cartilage formation is observed four weeks following implantation of bBMP at the cartilage defect, eight weeks (i.e., 2 months) after implantation, the bone formation had advanced to result in the complete closure of the defect (see, page 326, col. 2, to page 328, col. 1). Therefore, Cui confirms the teachings of Luyten that cartilage formation is only temporary. And, the combination of Cui and Luyten teaches away from applicant's invention.

Celeste discloses that BMP-12 and BMP-13, either alone or in combination with other BMPs, induce tendon/ligament-like tissue healing and repair. Celeste discloses that BMP-12 implanted rats showed tendon/ligament-like tissue formation but no cartilage or bone formation, whereas BMP-2 implanted rats showed only the expected cartilage and bone formation. Nothing in Celeste teaches or suggests that the cartilage formation is permanent such that the permanent cartilage is stable and not

subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device, as is recited in the amended claims.

Accordingly, nothing in the combination of Luyten, Celeste or Cui, teaches a method for repairing nonarticular cartilage tissue or promoting chondrogenesis at a nonarticular defect locus by inducing functional permanent cartilage tissue wherein the permanent cartilage is stable and not subject to resorption as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device undergo resorption, as recited in the amended claims of this application. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

Claims 1-6, 8-25, 27 and 30-34

The Examiner has maintained the rejection of claims 1-6, 8-25, 27 and 30-34 under 35 U.S.C. § 103(a) as being obvious over Cui in view of Celeste.

As discussed above, the claims of the instant application require the replacement of functional permanent cartilage tissue that is stable and not subject to resorption, as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device. This feature is not disclosed or suggested by Celeste or Cui, either alone or in combination. In fact, the combination teaches away from the claimed invention.

As discussed above, Cui discloses that bovine BMP induces new bone, not cartilage, to fill the defect in the cartilage, not functional permanent cartilage that is stable and not subject to resorption, as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device, as recited in the amended claims of the instant application. And, nothing in Celeste provides any teaching or suggestion that the recited osteogenic proteins claimed in the instant application are capable of inducing permanent replacement cartilage tissue that is stable and not

subject to resorption, as evidenced by the continued existence of cartilage at 4 months post implantation of the osteogenic device.

Thus, nothing in the combination of Cui or Celeste, teaches or suggests the claimed methods of the instant application. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

CONCLUSION

In view of the foregoing remarks, applicants request that the Examiner favorably reconsider this application and allow the claims pending herein.

Respectfully submitted,

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